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09/987,455	11/14/2001	Jiradej Manosroi	0652.2190001/EKS/Y-W	6739

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EXAMINER

NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 09/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
**09/987,455**

Applicant(s)  
**Manosroi et al.**

Examiner  
**Nashaat T. Nashed**

Art Unit  
**1652**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jul 25, 2003
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above, claim(s) 25-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 and 31-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some\* c) ☐ None of:  
1. ☒ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4 & 9 6) ☐ Other: \_\_\_\_\_

Applicant's election without traverse of Group I, claims 1-24 and 31-37, in Paper No. 11 is acknowledged. Thus, claims 25-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions of Groups II and III, there being no allowable generic or linking claim.

Claims 1-24 and 31-37 are pending and under consideration in this Office action.

The disclosure is objected to because of the following informalities:

- (a) The specification contains references to specific amino acid residues without identifying the amino acid sequence with a sequence identification number, see for example, page 4, paragraph 10; page 13, paragraph 49; and page 29, paragraph 100.
- (b) The specification contains nucleic/amino acid sequences without sequence identification numbers and identified by commercial data bases accession numbers, see for example page 11, paragraph 40; page 15, paragraph 54; page 20, paragraph 67; and page 25, paragraph 87. Since commercial data bases may change their accession number without referencing the original accession numbers, the use of commercial data bases accession numbers in the specification or the claim is not permitted.
- (c) The Figure 4 contains nucleic acid sequences which are not identified by sequence identification number in the Figure or the Figure description.
- (d) The signal peptide "OmpA" and the protein "gpIII" are not defined in the specification by a sequence identification numbers. Said polypeptide and protein appear to be specific polypeptide and protein and contain more than four amino acid residues, and therefore must be identified by a sequence identification number at each occurrence in the specification.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The specification and the claims contain nucleic and amino acid sequences described by the sequences and sequences identification numbers. Since the sequence listing is part of the specification, identifying the amino and nucleic acid sequences by sequence identification number is sufficient to describe said sequences to minimize typographical errors. Thus, it is recommended that applicants delete the sequences from the specification and the claims.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification lacks a sufficient written description for enablement based on deposit requirement.

The invention appears to employ the novel phagemid pComb3HSS. Since the phagemid is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed phagemid sequences is not fully disclosed, nor have all the sequences required for its construction been shown to be biblically known and freely available. The enablement requirement of 35 U.S.C. § 112 may be satisfied by deposit of the phagemid. The specification does not disclose a repeatable process to obtain the phagemid and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of the plasmid should have been made in accordance with 37 C.F.R. § 1.801-1.809.

If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicant, or a statement by an attorney of record over his/her signature and registration number, stating that a specific microorganism has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. § 1.801-1.809, the applicant may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his/her signature and registration number, showing that:

- (1) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (2) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;
- (3) the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
- (4) the deposit will be replaced if it should ever become inviable.

Claims 6 and 33 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-15, 17-24 and 31-37 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrases "a tPA variant", "a K2S variant" in claims 1, 2, 4, 10 and 11; "or a functional derivative thereof" in claims 1, 2, 12, and 14; "or a variant due to the degenerate nucleotide code" in claims 7, 12, and 15; "functional variant thereof" in claims 7 and 15; "OmpA" in claims 1, 2, 4, 5, and 14 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The OmpA appears to be a signal peptide comprising more than four amino acid residues and must be identified by a sequence identification number.
- (b) The phrases "DNA-derived" and "an active and correctly folded protein" in claim 1 render the claim indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Recombinantly produced proteins are not derived from DNA. They are derived from a host cells expressing recombinant DNA. For examination purposes only, the phrase "DNA-derived" is deleted from the claim and the phrase "an active and correctly folded protein" is assumed to mean "a thrombolitically active and correctly folded protein".
- (c) Claims 1-3, and 5-14 are incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (a) transforming a prokaryotic host cell with an expression vector comprising a DNA encoding the signal peptide OmpA of SEQ ID NO: X fused at the 3' end to the 5' end of a DNA sequence encoding tissue plasminogen activator (tPA), .....; (b) culturing the host cell under condition suitable for the expression of the protein product of said DNA; and (c) purify the extracellularly produced and a proteolytically and thrombolitically active protein.
- (d) The phrase "operably linked" in claim 1 renders the claimed method inoperable. One of ordinary skill in the art would interpret the phrase as two DNA sequences encoding two polypeptide in an expression vector under the control of the same promoter. The protein product of such a vector could be either a fusion protein or two different polypeptide. If the product is a fusion protein, the claimed method is operable. In contrast, if the product is two different polypeptide, the claimed method would be inoperable.

- (e) The phrases "DNA coding gpIII" in claims 4, and 5, and "gpIII protein" in claim 33 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The claim is referring to a specific DNA encoding a specific protein which is not defined by the claim or the specification and one of ordinary skill in the art would not know the identity of said protein. Applicant must insert an appropriate sequence identification number at each occurrence of "gpIII" in the claims. In addition, the phrase in claim 5 renders the claimed method inoperable because the result of expression of the nucleic acid would be expected to be a fusion protein comprising tPA and gpIII.
- (f) The phrase "pComb3HSS phagemid" in claims 6 renders the claimed method confusing and inoperable. The specification has not identified either the method of constructing pComb3HSS phagemid or its source. For examination purposes, the phagemid is presumed to be novel. With regard to claim 6, the pComb3HSS phagemid is assumed to be a blank vector and does not contain the coding sequence for any of the proteins which are intended to be made by the claimed method such as tPA or K2S.
- (g) Claims 7-9 do not end with a period which renders the claims incomplete and indefinite. The insertion of periods at the end of each claim would vacate this rejection.
- (h) Claims 11 and 17-20 contains references to a polypeptide fragments from a specific protein without identifying the protein with a sequence identification numbers which renders the claim indefinite. For examination purposes only, it assumed that the fragments are from SEQ ID NO: 19.
- (i) The phrase "a functional variant thereof or variant due to the degenerate nucleotide code" in claim 15 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes, the phrase is assumed to mean "a nucleic acid encoding the polypeptide encoded by the nucleic acid of SEQ ID NO: 5.
- (j) The phrase "operably linked" in claims 2 and 14 leads to multiple possible interpretations of the claims which render the claimed method indefinite, confusing, and inoperable. One of ordinary skill in the art would interpret the phrase as two DNA sequences encoding two polypeptide in an expression vector under the control of the same promoter. The protein product of such a vector could be either a fusion protein or two different polypeptide.
- (k) The phrase "hybridizing under stringent conditions" in claim 21 and 23 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. There are several sets of conditions known in the prior art as stringent conditions two

of which are exemplified in the specification in paragraph 52 on page 14. The DNA molecule obtained from one hybridization conditions could differ from another obtained under different stringent hybridization conditions. Since the specification only exemplify the hybridization conditions and the claim does not define a specific stringent hybridization conditions, one of ordinary skill in the art would not be able to define the metes and bounds of the claimed DNA molecule.

- (l) Claim 22, 24, 31, 32, and 34-37 are included with these rejections because they are dependent on rejected claims and do not cure the deficiencies of the claim from which they are dependent.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 8-10, 14, 21-23, 31, 32, and 34-37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Georgiou *et al.* [U. S. Patent 6,027,888 (888)].

The 888 patent teaches and claims a method of expression tissue plasminogen activator (tPA) in soluble and biologically active form in *E. coli*, see the abstract and claims 1-3, 18-22 and 28-40. It teaches a nucleic acid sequence encoding human tPA fused to OmpA signal peptide under the control of the lac promoter (claims 14, 31, 32, and 34-37, see the paragraph bridging columns 6 and 7, and column 7. Specifically, it teaches the invention can utilize any signal peptide, in particular *E. coli* alkaline phosphatase OmpA signal sequence which export a fusion protein to the bacteria periplasm, or outer membrane or to the culture supernatant in which such a cell is grown, see column 8, lines 21-63. The most preferred embodiment of the invention for the preparation of tPA comprises the transformation of *E. coli* SF103 cells with the expression vectors pTPA177 and pLppsOmpArPDI wherein the vector pTPA177 contains the OmpA leader tPA gene fusion (claims 1, 3, 8-10, and 21-23), see the paragraph bridging column 9 and 10.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-3, 7-24, 31, 32, and 34-37 are rejected under 35 U.S.C. § 103 as being unpatentable over Raymond *et al.* (IDS Document AM1: EP 0357391 A2) in view of Obukowicz *et al.* (IDS reference AR9: Biochemistry 1990, 29, 9737-9745), Niwa *et al.* [U. S. Patent 5,840,533 (533)] and the well known nucleic acid encoding human tissue plasminogen activator.

Raymond *et al.* teach an expression system for the production of heterologous proteins in *E. coli* comprising a transformed *E. coli* with a vector comprising a nucleic acid encoding said heterologous protein fused in frame to a nucleic acid sequence encoding the OmpA signal peptide to enable the secretion of the product protein, see abstract. In Figure 1, they teach a construct comprising the Tac promoter, lac operator, ribosomal binding domain, OmpA signal peptide coding sequence followed by in frame multiple restriction sites. They report the surprise excretion of properly folded and active heterologous protein into the medium upon the expression of the construct shown in Figure 1 comprising a coding sequence for a heterologous protein, see the last sentence on page 2, and the first full paragraphs on page 3 and page 4, First paragraph, and recommend their vector and host cell to produce human protein having therapeutic values such as growth factor, lymphokines, hormones, interferones, enzymes and the like, see page 3, lines 50-58. In addition, they teach method of making various eukaryotic proteins including human proteins in *E. coli*. Raymond *et al.*, however, failed to teach or suggest specifically the use of their method for making tissue plasminogen activator (tPA) and its fragment K2S.



Obukowicz *et al.* teach the expression of the K2S protein in *E. coli* by transformin the *E. coli* with a vector comprising a coding sequence K2S fused in frame to a coding sequence of PhoA leader peptide, see abstract.

The 533 patent several variants of human tPA and defined by the general for of SEQ ID NO: 1 which include the hexapeptide SEGNSD, identical to SEQ ID NO: 10 encoded by SEQ ID NO: 1 of the instant application, at its N-terminus, see column 1 and 2. The tPA variants can be obtained in an active form by expression in bacterial cell such as *E. coli* and display longer half-life and stronger thrombolytic activity. Specifically, it teaches the nucleic acid sequence of SEQ ID NO: 44 encoding the peptide SEGNSD fused to the N-terminus of K2S. The nucleic acid sequences of SEQ ID NO: 2, 4, 5, and 7 of the instant application comprising the entire nucleic acid sequence of SEQ ID NO: 44 of the patent without the initiation codon at its 5'-end. Also, it teaches the inclusion of a signal peptide in the DNA construct to express the t-PA variants, see column 5, lines 13 and 14.

The surprize observation of Raymond *et al.*, that a heterologouse protein expressed in *E. coli* and using their expression system is secreted to the culture medium properly folded and biologically active, would have motivated one of ordinary skill in the art to addopt said method for the production of the therapeutically important tPA and its enzymatically active fragments such as K2S by the method described by Raymond *et al.* Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to make the plasmid taught in Figure 1 of Raymond *et al.* and insert a nucleic acid encoding tPA or K2S taught by Obukowicz *et al.* to be expressed in frame with the OmpA signal peptide (claim 14), insert the plasmid in a vector (claims 31 and 32), and transform a host cell as taught by Raymond *et al.* (claims 34-37). It should be noted that the method is applicable to all the known fragments of tPA which have thrombolytic activity such as residues 87-527 (claim 17), residues 174-527 (claim 18), residues 180-527 (claim 19) and 220-527 (claim 20) of human tissues plasminogen activator. Also, the plasmid and the vector constructed by the ordinary skill in the art would be expected to hybrdize to the nucleic acid seugnce of SEQ ID NO: 6 which is the coding sequence for the OmpA signal peptide (claims 21 and 22) and to SEQ ID NO: 7 which contain the coding sequence of K2S polypeptide.

The 533 patent provide one of ordinary skill in the art with motivation to obtain the variant taught in the patent in large quantity as it teaches longer half-life time of the variants and greater thrombolytic activity. Also, the 533 patent suggests the expression of the variants in *E. coli* fused to a signal peptide for translocation of the variant tPA. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to attach the coding sequence OmpA the nucleic acid SEQ ID NO: 44 without the ATG initiation codon by well known methods in the art and inserted in well known vector under

the control of the well known lac operator, transform a host *E. coli* cell, and utilize the host cell in a method to make the variant tPA as taught by Raymond *et al.* It should be noted that the nucleic acid constructed by the ordinary skilled in the art would contain the nucleic acid of SEQ ID NO: 1 (claim 2) and has the nucleic acid sequence of SEQ ID NO's: 2, 4, 5 and 7 (claims 7, 12, 13, 15, 16, 23 and 24). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

Claims 11, 17-20 are rejected under 35 U.S.C. § 103 as being unpatentable over Georgiou *et al.* [U. S. Patent 6,027,888 (888)] in view of Obukowicz *et al.* (IDS reference AR9: Biochemistry 1990, 29, 9737-9745) and the well known nucleic acid encoding human tissue plasminogen activator and the kringle-2-serine protease (K2S) in the prior art.

The teachings of the 888 patent and Obukowicz *et al.* are summarized above.

Since many fragments and mutants of tPA have thrombolytic activity and are used for the treatment of vascular diseases in human, one of ordinary skill in the art would have been motivated to develop a recombinant method to prepare a thrombolytic fragment such as K2S in a large quantity. Thus, it would have been obvious to one of ordinary skill in the art to adopt the method taught in the 888 patent for making tPA to make the pharmaceutically important fragment K2S. The ordinary skill in the art would have replaced the coding sequence for tPA with the coding sequence for K2S in the vector pTPA177 which contains the OmpA leader sequence and express, transform an *E. coli* host cell and express the vector as taught in the 888 patent to obtain the properly folded and enzymatically active enzyme. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 6 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 8 of copending Application No. 09/987,457. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 7-24 and 31-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-11 of copending Application No. 09/987,457 (457). Although the conflicting claims are not identical, they are not patentably distinct from each other because independent claim 1 of the instant application and that of 457 application are nearly identical except for the identity of the protein being made. Claim 1 of the instant application is drawn to a process of recombinantly making tissue plasminogen activator (tPA) and a polypeptide consist of kringle-2, the protease domain of tPA (K2S), and variants thereof. In contrast, claim 1 of the 457 application is drawn to making any heterologus protein, presumably, heterologus to the host cell.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is

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(703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Nashaat T. Nashed, Ph. D.  
Primary Examiner